REMARKS

New figures are being provided to replace the figures filed with the response dated February 11, 2003. Applicants note that some of the previous figures were mislabeled relative to the original drawings and some sequences were inadvertently truncated. Applicants apologize for any confusion this may have caused. All figure legends have been deleted from the accompanying drawings.

Claims 34-47, 49-55 and 57-63 have been amended to track the language of independent claims 31, 48 and 56 from which these claims depend.

In the Advisory Action dated September 11, 2003, the Examiner requested support for the amino acid sequences recited in the claims presented August 25, 2003. Support for these sequences (as well as the sequences recited in the amended claims) can be found in Figures 1A-1G and 2A-2G which present the amino acid sequences for the heavy chains and light chains, respectively. The sequence identifiers recited in the claims correlate to these amino acid sequences.

Please direct all further written communications regarding this application to:

Alisa Harbin, Esq.
CHIRON CORPORATION
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

Date: 10/13/03

Respectfully submitted,

By: _____

Roberta L. Robins
Reg. No. 33,208

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Tel: (650) 493-3400
Fax: (650) 493-3440

AMENDMENTS TO THE CLAIMS

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1-30. (Canceled)

31. (Previously presented) An isolated nucleic acid molecule encoding a human Fab molecule, wherein the nucleic acid molecule comprises:

a first nucleotide sequence encoding a first polypeptide that is a binding portion of a γ1 heavy chain variable region (V_H) of said human Fab molecule where said heavy chain region exhibits immunological binding affinity for a hepatitis C virus (HCV) E2 antigen; and wherein the first polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7; and

a second nucleotide sequence encoding a second polypeptide that is a binding portion of a κ light chain variable region (V_L) of said human Fab molecule where said light chain variable region exhibits immunological binding affinity for a hepatitis C virus (HCV) E2 antigen, and wherein the second polypeptide comprises a sequence selected from the group consisting of SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14, and wherein said Fab molecules have binding affinity greater than 1×10^7 M^{-1} for HCV E2.

32. (Previously presented) The nucleic acid molecule of claim 31, further comprising:

a third nucleotide sequence encoding a first leader sequence peptide, wherein said third nucleotide sequence is operably linked to the 5' terminus of the first nucleotide sequence and is capable of causing secretion of the encoded heavy chain variable region when the encoded heavy chain variable region and the first leader sequence peptide are expressed; and

a fourth nucleotide sequence encoding a second leader sequence peptide, wherein said fourth nucleotide sequence is operably linked to the 5' terminus of the second nucleotide

sequence and is capable of causing secretion of the encoded light chain variable region when the encoded light chain variable region and the second leader sequence peptide are expressed.

33. (Original) The nucleic acid molecule of claim 32, wherein the third and fourth nucleotide sequences are selected from the group of leader sequences consisting of *omp* A and *pel*B.

34. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4A (SEQ ID NO:22)~~ shown as SEQ ID NO: 1.

35. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4B (SEQ ID NO:23)~~ shown as SEQ ID NO: 2.

36. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4C (SEQ ID NO:24)~~ shown as SEQ ID NO: 3.

37. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4D (SEQ ID NO:25)~~ shown as SEQ ID NO: 4.

38. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4E (SEQ ID NO:19)~~ shown as SEQ ID NO: 5.

39. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4F (SEQ ID NO:26)~~ shown as SEQ ID NO: 6.

40. (Currently amended) The nucleic acid molecule of claim 31, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4G (SEQ ID NO:27)~~ shown as SEQ ID NO: 7.

41. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 3A (SEQ ID NO:15)~~ shown as SEQ ID NO: 8.

42. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 3B (SEQ ID NO:16)~~ shown as SEQ ID NO: 9.

43. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 3C (SEQ ID NO:17)~~ shown as SEQ ID NO: 10.

44. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 3D (SEQ ID NO:18)~~ shown as SEQ ID NO: 11.

45. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted Figure 3E (SEQ ID NO:19)~~ shown as SEQ ID NO: 12.

46. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 3F (SEQ ID NO:20)~~ shown as SEQ ID NO: 13.

47. (Currently amended) The nucleic acid molecule of claim 31, wherein the second ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 3G (SEQ ID NO:21)~~ shown as SEQ ID NO: 14.

48. (Previously presented) An isolated nucleic acid molecule, comprising a first nucleotide sequence encoding a binding portion of a γ1 heavy chain variable region (V_H) of a human Fab molecule obtained from a combinatorial library, wherein said Fab molecule exhibits immunological binding affinity greater than 1 x 10^7 M^{-1} for a hepatitis C virus (HCV) E2 antigen and further wherein the γ1 heavy chain sequence is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7.

49. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4A (SEQ ID NO:22)~~ shown as SEQ ID NO: 1.

50. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4B (SEQ ID NO:23)~~ shown as SEQ ID NO: 2.

51. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4C (SEQ ID NO:24)~~ shown as SEQ ID NO: 3.

52. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4D (SEQ ID NO:25)~~ shown as SEQ ID NO: 4.

53. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4E (SEQ ID NO:19)~~ shown as SEQ ID NO: 5.

54. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4F (SEQ ID NO:26)~~ shown as SEQ ID NO: 6.

55. (Currently amended) The nucleic acid molecule of claim 48, wherein the first ~~nucleotide~~ polypeptide sequence is ~~depicted in Figure 4G (SEQ ID NO:27)~~ shown as SEQ ID NO: 7.

56. (Previously presented) An isolated nucleic acid molecule, comprising a first nucleotide sequence encoding a binding portion of a κ light chain variable region (V_L) of a human Fab molecule obtained from a combinatorial library, wherein said Fab molecule exhibits immunological binding affinity greater than 1×10^7 M^{-1} for a hepatitis C virus (HCV) E2 antigen and further wherein the κ light chain sequence is selected from the group consisting of SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13 and SEQ ID NO:14.

57. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence ~~depicted in Figure 3A (SEQ ID NO:15)~~ is shown as SEQ ID NO: 8.

58. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence is ~~depicted in Figure 3B (SEQ ID NO:16)~~ shown as SEQ ID NO: 9.

59. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence is ~~depicted in Figure 3C (SEQ ID NO:17)~~ shown as SEQ ID NO: 10.

60. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence is ~~depicted in Figure 3D (SEQ ID NO:18)~~ shown as SEQ ID NO: 11.

61. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence is ~~depicted in Figure 3E (SEQ ID NO:19)~~ shown as SEQ ID NO: 12.

62. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence is ~~depicted in Figure 3F (SEQ ID NO:20)~~ shown as SEQ ID NO: 13.

63. (Currently amended) The nucleic acid molecule of claim 56, wherein the ~~second nucleotide~~ κ light chain sequence is ~~depicted in Figure 3G (SEQ ID NO:21)~~ shown as SEQ ID NO: 14.

64. (Original) An expression vector, comprising the nucleic acid molecule of claim 31 operably linked to control sequences that direct the transcription of the first and second nucleotide sequences whereby said first and second nucleotide sequences can be transcribed and translated in a host cell.

65. (Original) The expression vector of claim 64, wherein the control sequences are capable of directing the transcription of the first and second nucleotide sequences in a prokaryotic host cell.

66. (Original) The expression vector of claim 64, wherein the control sequences are capable of directing the transcription of the first and second nucleotide sequences in a eukaryotic host cell.

67. (Original) An expression vector, comprising the nucleic acid molecule of claim 48 operably linked to control sequences that direct the transcription of the first nucleotide sequence whereby said first nucleotide sequence can be transcribed and translated in a host cell.

68. (Original) The expression vector of claim 67, wherein the control sequences are capable of directing the transcription of the first nucleotide sequence in a prokaryotic host cell.

69. (Original) The expression vector of claim 67, wherein the control sequences are capable of directing the transcription of the first nucleotide sequence in a eukaryotic host cell.

70. (Original) An expression vector, comprising the nucleic acid molecule of claim 56 operably linked to control sequences that direct the transcription of the first nucleotide sequence whereby said first nucleotide sequence can be transcribed and translated in a host cell.

71. (Original) The expression vector of claim 70, wherein the control sequences are capable of directing the transcription of the first nucleotide sequence in a prokaryotic host cell.

72. (Original) The expression vector of claim 70, wherein the control sequences are capable of directing the transcription of the first nucleotide sequence in a eukaryotic host cell.

73. (Original) A prokaryotic host cell transformed with the expression vector of claim 65.

74. (Original) A prokaryotic host cell transformed with the expression vector of claim 68.

75. (Original) A prokaryotic host cell transformed with the expression vector of claim 71.

76. (Original) A eukaryotic host cell transformed with the expression vector of claim 66.

77. (Original) A eukaryotic host cell transformed with the expression vector of claim 68.

78. (Original) A eukaryotic host cell transformed with the expression vector of claim 72.

79. (Original) A method of producing a recombinant human Fab molecule, comprising:
(a) providing a population of transformed host cells according to claim 76; and
(b) expressing said recombinant Fab molecule from the expression vector.

80. (Previously presented) A method of producing a recombinant polypeptide having a binding portion of a γ1 heavy chain variable region (V_H) of a human Fab molecule, comprising:

(a) providing a population of transformed host cells according to claim 77; and

(b) expressing said recombinant polypeptide from the expression vector.

81. (Previously presented) A method of producing a recombinant polypeptide having a binding portion of a κ light chain variable region (V_L) of a human Fab molecule, comprising:

(a) providing a population of transformed host cells according to claim 78; and

(b) expressing said recombinant polypeptide from the expression vector.

82-116. (Canceled)

117. (Previously presented) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1A (SEQ ID NO: 1) and the contiguous sequence of amino acids depicted in Figure 2A (SEQ ID NO: 5).

118. (Previously presented) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1B (SEQ ID NO: 2) and the contiguous sequence of amino acids depicted in Figure 2B (SEQ ID NO: 6).

119. (Previously presented) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1C (SEQ ID NO: 3) and the contiguous sequence of amino acids depicted in Figure 2C (SEQ ID NO: 7).

120. (Previously presented) The isolated nucleic acid molecule of claim 31, wherein the human Fab molecule encoded by the first and second nucleotide sequences comprises the contiguous sequence of amino acids depicted in Figure 1D (SEQ ID NO: 4) and the contiguous sequence of amino acids depicted in Figure 2D (SEQ ID NO: 8).

121. (Previously presented) An isolated nucleic acid molecule that encodes a recombinant human monoclonal antibody that exhibits immunological binding affinity for a hepatitis C virus (HCV) E2 antigen, wherein the antibody comprises at least one group of three complementarity determining regions (CDRs) interposed between framework regions (FRs) said FRs derived from a human immunoglobulin, wherein the group of three CDRs is selected from the group consisting of amino acid residue numbers 32-36, 51-71, 104-121 of SEQ ID NO:1; amino acid residue numbers 32-36, 51-67, 100-116 of SEQ ID NO:2; amino acid residue numbers 32-36, 51-67, 100-117 of SEQ ID NO:3; amino acid residue numbers 31-35, 50-66, 99-114 of SEQ ID NO:4; amino acid residue numbers 23-34, 49-56, 89-97 of SEQ ID NO:5; amino acid residue numbers 23-33, 49-55, 88-95 of SEQ ID NO:6; amino acid residue numbers 23-34, 50-56, 89-97 of SEQ ID NO:7; and amino acid residue numbers 23-33, 49-55, 88-96 of SEQ ID NO:8.

122. (Previously presented) The isolated nucleic acid molecule of claim 121, wherein the antibody encoded by the nucleic acid molecule comprises a first group of CDRs with amino acid residue numbers 32-36, 51-71, 104-121 of SEQ ID NO:1 interposed between FRs, and a second group of CDRs with amino acid residue numbers 23-34, 49-56, 89-97 of SEQ ID NO:5, interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

123. (Previously presented) The isolated nucleic acid molecule of claim 121, wherein the antibody comprises a first group of CDRs with amino acid residue numbers 32-36, 51-67, 100-116 of SEQ ID NO:2 interposed between FRs, and a second group of CDRs with amino acid residue numbers 23-33, 49-55, 88-95 of SEQ ID NO:6, interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

124. (Previously presented) The isolated nucleic acid molecule of claim 121, wherein the antibody comprises a first group of CDRs with amino acid residue numbers 32-36, 51-67, 100-117 of SEQ ID NO:3 interposed between FRs, and a second group of CDRs with amino acid residue numbers amino acid residue numbers 23-34, 50-56, 89-97 of SEQ ID NO:7 interposed

between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

125. (Previously presented) The isolated nucleic acid molecule of claim 121, wherein the antibody comprises a first group of CDRs with amino acid residue numbers amino acid residue numbers 31-35, 50-66, 99-114 of SEQ ID NO:4 interposed between FRs, and a second group of CDRs with amino acid residue numbers 23-33, 49-55, 88-96 of SEQ ID NO:8 interposed between FRs, wherein the first and second groups of CDRs interposed between FRs together form a binding site for an HCV E2 antigen.

126. (Previously presented) A method for providing an antibody titer to HCV in a mammalian subject, comprising introducing a therapeutically effective amount of the composition comprising the isolated nucleic acid of claim 120 to said subject.

127. (Previously presented) A method for providing an antibody titer to HCV in a mammalian subject, comprising introducing a therapeutically effective amount of the vaccine composition of claim 121 to said subject.

128. (Previously presented) An isolated nucleic acid molecule encoding a human Fab molecule, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, and SEQ ID NO:27.

129. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:15.

130. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:16.

131. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:17.

132. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:18.

133. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:19.

134. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:20.

135. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:21.

136. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:22.

137. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:23.

138. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:24.

139. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:25.

140. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:26.

141. (Previously presented) The isolated nucleic acid molecule of claim 128, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:27.